Claims 35, 39, 40, 44-48 and 52-54: Canceled

REMARKS

The applicants acknowledge the Office Action of July 1, 2003, with appreciation. To begin, the Office acknowledges Applicant's election of Group I, in Paper No. 5. The Office indicates the election as filed will be treated as an election *without traverse*. By designating the subject matter outside the elected group as being merely withdrawn pending notification of allowable subject matter, the applicants distinctly and affirmatively point out subject matter which they assert, upon examination will be found a part of the claimed invention. The applicants reassert their right to rejoin non-elected claims upon the identification of allowable subject matter.

Claims 34-72 are pending in the Application, of those, Claim 36, 37, and 55-71 were withdrawn from consideration. Claims 34, 35, 38-54 and 72 were rejected by the Office under 35 U.S.C §112, second paragraph, as being indefinite for failing to claim with particularity. Claims 34 and 72 were considered indefinite for use of the term "orienting". Claims 34 and 72 are presently amended to substitute the term "inducing", as kindly suggested by the Office. Additionally, Claims 34 and 72 are considered vague and indefinite for the use of the phrase "in which the Th1 response is close to or greater than the Th2 type response". Applicants note that the language "close to" finds Specificational support on page 3, lines 35-39. The language "or greater than" has been removed from the presently amended Claims 34 and 72. Additionally, Claims 34 and 72 were amended to further limit the instant invention to the use of a crude membrane fraction obtained from *K. pneumoniae* by a process of preparation, as disclosed in the Specification, which is mixed with an antigen or hapten to elicit the desired immune response.

Claim 38 was rejected for improper Markush language. The claim has been amended to conform to proper language, as kindly suggested by the Office. Similarly, Claim 51 was amended to define a proper Markush group.

Claim 41 was considered indefinite for the use of the term "capable of". Similarly, Claim 42 was considered indefinite for use of the term "derived from". Objectionable language has been removed from Claims 41 and 42, thereby providing the requested definition.

Claim 43 and Claim 48 were rejected for improper use of the language "genetic recombination". Applicants submit the language "recombinant technologies" as a more appropriate term. Using recombinant technologies for heterologous protein expression to form proteinaceous complexes finds Specificational support on page 10, lines 16-29.

Claim 49 is rejected for the language "carry the membrane fraction...in a form...which makes it possible to enhance..." Applicants have amended the claim and removed the objectional language, "makes it possible". Applicants submit that these amendments provide the requested definition.

Moving on to the prior art rejections, the Office rejects claims 34, 38-40, 44, 48 and 72 under 35 USC §102(b) as being anticipated by Rauly, et al., (Research in Immunology, Vol. 149 No. 1, pg.99, January 1998) which discloses the use of a homogeneous preparation of recombinant *K. pneumoniae* P40 protein as an immunopotentiator. When coupled to a B-cell epitope derived from RSV, the resulting complex induces a mixed Th1/Th2 response when administered to animals. The instant invention as claimed limits the Th1 type response to be close to the Th2 response, as defined in the Specification. Applicants acknowledge Rauly, et al. decribes a mixed immune response following immunization with P40-hapten preparations. However, there is no disclosure of the magnitude of the Th1 response of the mixed response obtained using recombinant P40. Applicants invite the Office to consider the disclosure of the cited Binz, et al., (US Patent 6,197,929; column 10, lines 36-47, Table 4) wherein the mixed immune response following immunization with the P40-hapten is characterized in detail with respect to the antibody isotypes. The mixed immune response elicited following immunization with the P40-hapten is one in which the Th1 response, particularly IgG2a and IgG3 isotypes, is significantly less than the Th2 response, particularly IgG1 and IgG2b isotypes. Applicants submit that the Office has not made an adequate demonstration of anticipation or provided a demonstration that Rauly, et al. suggests the instant invention. Applicants have demonstrated that immunization with the instant crude membrane fraction, FMKp, elicites a preferred immune response, one in which the Th1 response is close to the Th2 response. Such Th1/Th2 profile having a Th1 specific response close to the Th2 response is desired particularly to avoid an essentially Th2 response which poses problems in subjects with allergic predisposition (pg. 2, lines 15-29 of the Specification).

Applicants also note that Rauly, et al. adeptly demonstrates carrier-related differences in the immune response generated against the same antigen or hapten. The rP40-G1' conjugate generated a mixed Th1/Th2 repsonse, in contrast to tetanus toxoid-G1' conjugate, which induced a Th2-like type of response. Claim 34 and Claim 72 have presently been amended to further limit the instant invention to the use of a crude membrane extract from *K. pneumoniae,* FMKp, obtained by a defined process of preparation, to be used as a carrier to elicit the claimed immune response. The crude membrane preparation is materially distinct from a purified, recombinant P40 protein preparation. As demonstrated by Rauly, et al. differences in the carrier protein affect the immune response directed to a particular antigen or hapten. Consequently, the reference may not be relied upon for the teaching that *K. pneumoniae* membrane carriers can be expected to induce uniform responses, much less the instant, mixed immune response. The reference does not suggest the performance of the crude membrane fraction, FMKp, when mixed with an antigen or hapten, would result in the claimed immune response. Based upon these analyses, Applicants submit that the instant invention is not anticipated, nor made obvious by the disclosure of Rauly, et al.

The Office goes on to reject Claims 34, 38-41, 43-54, 48-49 and 72 under 35 USC §102(e) as being anticipated by Binz, et al., (US Patent 6,197,929). The reference also discloses the use of recombinant *K. pneumoniae* P40 protein as an immunopotentiator, as well as *K. pneumoniae* protein that was purified through chromatographic techniques to obtain a homogeneous P40 preparation, free from other contaminating membrane components. The immune response was evaluated following immunization with covalent P40/hapten complexes (P40ext). The Office draws attention to a Th1 response, which is generated in animals, and is exemplified by the production of a highly quantitative delayed hypersensitivity response and macrophage activation. Applicants acknowledge these analyses and further consider the indepth analysis of the antibody isotype distribution that defines a Th1 type response and a Th2 type response following P40 immunization. The reference indicates that the titer of Th1 isotype antibodies, particularly IgG2a and IgG3, is much lower than the titer of Th2 isotype antibodies, particularly IgG1 and IgG2b and IgE (column 10, lines 36-47, Table 4). This is in stark contrast to the instant invention, as recited in Claims 34 and 72, which results in a "mixed Th1/Th2 response directed against an antigen or hapten, in which response the Th1 response is close to the Th2 response" following immunization with a mixture of FMKp/hapten. The Office has not made a *prima facie* demonstration that one skilled

in the art would expect the capacity of the instant crude membrane fraction to induce the claimed response which is characterized by the distinguishing Th1/Th2 mixed response, wherein the Th1 response is close to the Th2 response. Therefore, Applicants submit that the instant invention is not anticipated, nor made obvious, by the disclosure of Binz, et al., (US Patent 6,197,929).

Finally, the applicants note again that the references cited by the Office pertain to the use of specifically P40 protein preparations which are recombinantly expressed and purified or are purified to homogeneity from *K. pneumoniae* using extensive chromatographic techniques. These preparations are materially distinct from the composition of the crude membrane preparation of the instant invention. Neither reference suggests the performance of the claimed crude membrane preparation as an immunopotentiator. The former Claims 34 and 72 are presently limited to immunization with the crude membrane fraction, mixed with an antigen or hapten, to generate a preferred type of immune response, directed against the antigen or hapten. The cited references disclose only P40 protein preparations that are covalently coupled or combined with an antigen or hapten, which are capable of inducing a mixed Th1/Th2 response. Additionally, neither reference demonstrates, nor suggests, the claimed immune response, one in which the Th1 response is close to the Th2 response, as defined in the Specification of the instant invention, can be obtained using P40 protein as a carrier.

Applicants submit that these cited references actually sustain the novelty of the instant invention. Rauly, et al. demonstates that different carrier proteins have a differential affect on the type of immune response elicited to a singular antigen or hapten. Considering Binz, et al. the immune response elicited by immunization with purified P40 teaches away from the claimed mixed response of the instant invention. Neither reference suggests or anticipates the performance of the crude membrane fraction, FMKp, mixed with antigen or hapten, could elicit the preferred immune response, in which the Th1 response is close to the Th2 response. In light of these remarks, reconsideration and withdrawal of the prior art rejection is respectfully solicited.

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Accordingly, entry of the present amendment, reconsideration of all grounds of rejection, withdrawl thereof and passage of this application to issue are all thereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,
THE FIRM OF HUESCHEN AND SAGE

By: _____
G. PATRICK SAGE, Attorney #37,710

Dated: 12/1/2003
Customer No.: 25,666
500 Columbia Plaza
350 East Michigan Ave.
Kalamazoo, MI 49007-3856
(269) 382-0030
GPS/KLW

Enclosure: Listing of Claims, Extension Fee (Two months) $420.00 and Postal Card Receipt

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.